Computers in Biology and Medicine 91 (2017) 306–317

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/compbiomed

Web-based accurate measurements of carotid lumen diameter and stenosis severity: An ultrasound-based clinical tool for stroke risk assessment during multicenter clinical trials

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ARTICLE INFO

Keywords:
Stroke
Carotid arteries
Ultrasound
Cloud-based
Lumen diameter
Stenosis
Total lumen area

ABSTRACT

Background: This pilot study presents a completely automated, novel, smart, cloud-based, point-of-care system for (a) carotid lumen diameter (LD); (b) stenosis severity index (SSI) and (c) total lumen area (TLA) measurement using B-mode ultrasound. The proposed system was (i) validated against manual reading taken by the Neurologist and (ii) benchmarked against the commercially available system.
Method: One hundred patients (73 M/27 F, mean age: 68 ± 11 years), institutional review board approved, written informed consent, consisted of left/right common carotid artery (200 ultrasound scans) were acquired using a 7.5-MHz linear transducer.
Results: The measured mean LD for left and right carotids were (in mm): (i) for proposed system (6.49 ± 1.77, 6.66 ± 1.70); and (ii) for manual (6.29 ± 1.79, 6.45 ± 1.63), respectively and coefficient of correlation between cloud-based automated against manual were 0.98 ($P < 0.0001$) and 0.99 ($P < 0.0001$), respectively. The corresponding TLA error, Precision-of-Merit, and Figure-of-Merit when measured against the manual were: 4.56 ± 3.54%, 96.18 ± 3.21%, and 96.85%, respectively.
The AUC for the receiving operating characteristics for the cloud-based system was: 1.0. Four statistical tests such as: Two-tailed z-test, Mann-Whitney test, Kolmogorov-Smirnov (KS) and one-way ANOVA were performed to demonstrate consistency and reliability.
Conclusions: The proposed system is reliable, accurate, fast, completely automated, anytime-anywhere solution for multi-center clinical trials and routine vascular screening.

1. Introduction

Cardiovascular related diseases are the number one killer of human's worldwide, accounting for 17.3 million deaths per year, a number that is expected to grow to more than 23.6 million by 2030 [1]. This is caused by the progression of atherosclerosis disease [2] which leads to the blockage of the arteries (stenosis) [3], limiting the flow of oxygen-rich blood to the coronary artery and brain (Fig. 1), which in turn leads to myocardial infarction and stroke [4–6]. Unlike carotid intima-media thickness (cIMT) for preventive healthcare screening, rapid and accurate stenosis detection and computation of lumen diameter (LD) of the carotid arteries is vital for planning surgical procedures like carotid artery stenting (CAS) and endarterectomy (CEA) [7,8]. Since the plaque distribution is independent of the wall side (proximal vs. distal) and multi-focal [9], robust

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https://doi.org/10.1016/j.compbiomed.2017.10.022
Received 10 September 2017; Received in revised form 18 October 2017; Accepted 20 October 2017

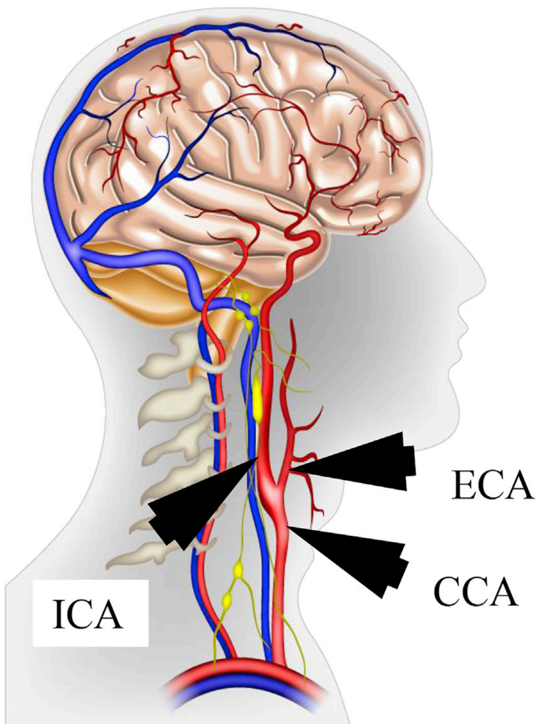

Fig. 1. Illustration of plaque formation in the carotid artery (Courtesy of AtheroPoint™, Roseville, CA, USA. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

LD/Stenosis methods need to be developed for better characterization for risk assessment [10]. The main objective of this study is to propose a completely automated, smart, point-of-care system for LD/Stenosis measurement using B-mode ultrasound (BMUS).

Several medical imaging modalities have been adopted for imaging arterial stenosis such as ultrasound (US), CT and MRI [5]. The US offers several advantages such as its ability to image lesions non-invasively, the presence of no radiation, user-friendly and real-time [11,12]. Doppler ultrasound is currently adopted to compute the percentage of stenosis severity. This is based on pulse wave velocity which in turn uses the assumption that arteries have constant stiffness [13,14]. This assumption may not always be valid, and therefore not accurate for LD/Stenosis measurement. Further, it does not use image-based features which are a true representation of the image reconstruction. Another way of computing LD/stenosis is manual tracing which is tedious and shows large intra- and inter-observer variability [11,15]. Innovations such as compound and harmonic imaging in recent years have made it possible to automatically compute the LD/Stenosis [16].

Recently, the automated image-based LD detection techniques have started to emerge. Saba et al. [17] compared the strength of correlation between carotid LD and inter-adventitial diameter (IAD) with plaque score (PS). Carotid IAD was found to be more strongly correlated to PS than carotid LD. The study did not mention stenosis measurement. Dey et al. [18] computed the carotid LD all along the carotid artery while studying the effect of watermarking algorithms and its recovery of the watermarks for stroke applications. Further, Ikeda et al. [19] investigated the LD detection for computing the location of (a) carotid bulb and (b) CCA bifurcation, so the LD can be measured from this location point. Recently Suri's team [16] detected the carotid lumen and LD measurement by fusing regional and boundary information.

The systems discussed above are most prone to challenges since they lack user-control, which is highly desirable in low resolution or poor image acquisition protocols. It is very crucial to have mitigation tools controlled by the physician or sonographer, thus the concept of semi-automated system design is missing, especially when there are spikes or bumps in the wall interfaces [16]. Second, previous methods do not focus on image-based stenosis severity index (SSI) measurement and lack of accurate blood flow regions such as total lumen area (TLA). Third, the above systems lack the concept of telemedicine-based models [20], as a result, one is confined to the operating room or emergency rooms or preventive healthcare rooms.

The proposed study removes all the above weaknesses by adopting a web-based model designed earlier for the plaque burden measurement [6]. Using the same spirit, we design and develop a combined image and web-based LD detection and LD measurement system (so-called AtheroCloud), followed by SSI and TLA computations. The image-based LD system is more challenging in the sense that the near wall interfaces are crucial for estimation of LD, SSI, and TLA, which brings in the novelty. The current study is focused on: (a) design and development; (b) validation against the manual readings (as traced by the Neurologist) and (c) benchmarking against the desktop-based systems. Note the overall system provides the complete experimental protocol and statistical analysis as developed along the spirit of the cloud-based cIMT system [21]. Further, based on NASCET criteria, the current AtheroCloud system computes the SSI in both automated and semi-automated combined image and web-based frameworks. Lastly, our study shows comprehensive performance evaluation against the gold standard and benchmarking against the commercially available desktop system.

2. Material and methods

Two hundred four (204) patients from July 2009 to December 2010 underwent B-mode carotid ultrasound scans. A total of 407 ultrasound scans (one patient had one image missing) from both left and right CCA artery were obtained from Toho University, Japan (Ethics approved with IRB). For this pilot study, due to manual tracing and cost compulsion, we randomly selected 100 patients (200 CCA ultrasound scans). No special criteria were adopted in choosing these 100 patients (73 M/27F). Mean age: 68 ± 11 years. Of these, 50 patients had proximal lesion location, 29 at middle and 21 at a distal location. These 100 patients (42 smokers) had a mean HbA1c, LDL, HDL, total cholesterol as: 6.40 ± 1.2 (mg/dl), 103.96 ± 31.34 (mg/dl), 51.17 ± 14.04 (mg/dl) and 179.60 ± 38.61 (mg/dl), respectively.

All the patients, written informed consent, were scanned using ultrasound scanner (Aplio XV) equipped with 7.5 MHz linear array transducer from Toshiba, Inc. Tokyo, Japan. Same sonographer (having an experience of 15 years) scanned all the patients. Average resolution: 0.0529 mm/pixel.

2.1. Manual lumen diameter reading

For performance evaluation of AtheroCloud software system, a gold standard was adopted by manually tracing the lumen-intima (LI) interface of the near and far walls of the carotid artery. These manual borders were traced by an experienced Neurologist (L.S) using a commercial software package ImgTracer™ (courtesy of AtheroPoint™, Roseville, CA, USA) as shown in Fig. 2. The top red line indicates the LI interface for the near wall and the bottom red line indicates the LI interface for the far wall. The ImgTracer™ software has been successfully used for several anatomic applications all around the world. Recently Suri and his team [6] have used this software (ImgTracer™) to generate the ground truth by manually tracings the LI interfaces of carotid arteries.

2.2. Workflow architecture of AtheroCloud ultrasound system

This pilot study is the first of its kind in which LD/TLA/SSI is automatically measured in carotid ultrasound scans in the cloud-based settings. The workflow is shown in Fig. 3. It is a three-layered architecture: (i) Graphical user interface layer: here, the doctor can interact with the